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RADIUM

EDITED BY
CHARLES H. VIOL, Ph. D.
AND
WILLIAM H. CAMERON, M. D.

VOL. XI APRIL, 1918 No. 1

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D. with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. XI APRIL, 1918 No. 1

REPORT OF RESULTS OF RADIUM TREATMENT AT THE COLLIS P. HUNTINGTON MEMORIAL HOSPITAL BY THE CANCER COMMISSION OF HARVARD UNIVERSITY*

By William Duane, Ph. D., Boston,
and
Robert B. Greenough, M. D., Boston.

The treatment of cancer and allied conditions by radium has now (June, 1917) been in operation at the Collis P. Huntington Memorial Hospital for a sufficient length of time to permit conclusions with regard to its value to be formulated. Radium was first employed here in September, 1913, and from that time to the present day has been the main interest and activity of the clinical work carried on by the Cancer Commission.

The chief responsibility for this work must be accorded to Dr. J. Collins Warren, Chairman of the Cancer Commission of Harvard University. Dr. Warren early saw the necessity for an independent and unbiased investigation of the value of the many therapeutic agents advocated from time to time as "cures" for cancer, and it is due entirely to his wise foresight, his unlimited enthusiasm, and his untiring effort that the hospital was established, and the clinical work of the Commission begun on a broad basis of scientific accuracy, and with resources sufficient to maintain these standards. During this period a number of different individuals have taken a part in the work, but owing to the very complete system of records and clinical notes established by the first Physician-in-Charge of the Hospital, Dr. Thomas Ordway, the data obtained are now available for study, and the results can be accumulated and stated with a considerable degree of accuracy. The hospital was opened during the period when Dr. E. E. Tyzzer was Director of the

* Reprinted from the Boston Medical Surgical Journal, CLXXVII, 359-365, September 13, 1917.

Cancer Commission, and he took a large part in the organization of the work, as well as the more definite responsibility for the pathological work, the reports of autopsies and the examination of clinical pathological material. The work with radium began in September, 1913, with the appointment to the Commission of William Duane, Ph. D., Research Fellow in Physics. Dr. Duane has had charge of the preparation and measurement of the radium, and of the details of its practical application to treatment of the cases adjudged suitable for radium therapy. In addition to Dr. Tyzzer, Dr. Ordway and Dr. Duane, a number of others have had a share in the collection of the data on which this report is based: Dr. Ellis Kellert and Dr. George Benet, resident physicians; Dr. Henry A. Christian and Dr. Francis Peabody, consulting physicians; Dr. J. Lucien Morris, Dr. F. S. Hammett, Dr. Henry Lyman, chemists; Dr. W. J. Kerr, Dr. Carl T. Harris, Dr. Clarence T. Hyman, house officers; Dr. Edward H. Risley and Dr. Channing C. Simmons, assistant surgeons; Dr. George A. Leland, Jr., Out-Patient surgeon; Dr. A. A. Ghoreyeb, Research Fellow in Pathology; Miss Irene W. Mason and Miss Anna Gibson, matron-superintendents of the hospital; and many consultants in special lines of clinical work, including Drs. Harvey Cushing, C. A. Porter, D. Crosby Greene, Harris P. Mosher, E. A. Crockett, W. P. Graves, George Derby, C. J. White, as well as Dr. Robert B. Greenough, Surgeon-in-Charge of the Huntington Hospital. All of above-mentioned persons have in some degree contributed to the accumulation of the material upon which this report is based.

The present organization of the hospital work is as follows: A patient is referred to the hospital by his own physician, or by another institution. Application cards are furnished with blanks for the principal data which it is desired to obtain. The patient is then examined with a view to the diagnosis and the question of whether or no radical operative treatment is a possibility. When the opinion of a consultant is needed the services of the members of the different departments of the Harvard Medical School are freely called upon, and have been most generously given. With the exception of certain minor superficial lesions of the non-metastasizing type, it has always been the policy of the hospital in operable cases, to advise operation, and to withhold radium or other non-operative treatment. If operation is considered advisable the patient is referred to one of the larger hospitals, or returned to his own physician with this opinion. A few cases have been received at the Huntington Hospital for radical operation, but they are taken only for special reasons, and are the exceptions to the general rule.

Pathological reports in confirmation of the diagnosis of cancer are sought in every case. In the cases of post-operative recurrence of cancer, the pathological report upon the tissue removed at operation can usually be obtained. In advanced inoperable and ulcerated cases, a fragment of tissue to confirm the diagnosis can usually be secured with the curette, without undue danger of spread of the disease. Where the tissues are unbroken, however, it has been the policy of the hospital to refrain from employing the exploratory excision of fragments of tissue, on the ground that the danger to the patient of artificial spread of the disease outweighed the advantages of a certain diagnosis. This rule has been broken, advisedly, from time to time, but only on rare occasions.

If the case is one which is considered suitable for radium treatment, the matter is discussed with Dr. Duane; the details in regard to dosage, screening, distance, duration and frequency are determined, and treat-

ment is begun. Special methods of application are devised for special cases, and the progress of the case is followed both by the radium expert, and by the surgeon. Data, consisting of measurements, photographs, tracings, etc., are made, and the record is continued. No case is discharged "cured" or otherwise, until terminated by death. A follow-up system, under Miss Ruth Symonds, the Social Service Worker of the hospital, has yielded excellent results in tracing up "lost" cases. From April, 1912, till January 1, 1916, out of 1080 cases, the end-results (to within six months) were known in all but 39.

It has been the policy of the hospital to restrict the use of radium to patients that could be brought to the hospital to be cared for by the staff; only in this way can the full benefit of the radium be secured to the patient, and the full benefit of the data obtained secured to the Commission.

In reporting the results of the use of radium in the treatment of cancer, some preliminary statements are advisable. When the first reports of the therapeutic use of radium were given out, a lapse of time sufficient for an unbiased and definite conclusion as to its benefits had not occurred. In certain clinics, also, the customary data for the surgical diagnosis of malignant disease in its different situations were not always obtained, and evidence in support of the statements that the cases treated were actually cancer was not provided. The sensational publications in the lay press relating to the wonderful effects of radium therapy, and the dramatic and interesting physical phenomena of radioactivity, all helped to rouse in the public, and among the profession at large, an expectation of brilliant results far in excess of what the facts now actually seem to warrant. Again, the obviously extravagant claims of some of the earlier exponents of radium therapy served to arouse in the more conservative members of the profession a natural pessimism, which led them to distrust its value altogether. As a fact the real truth lies somewhere between these two extremes. Radium is not a cure for all kinds of cancer. There are many cases of cancer in which it can be said to be of no material benefit; but there are also many cases where its use prolongs life, relieves distressing symptoms, improves the general condition and the functional activities of the patient, and mitigates, as does no other agent which we have employed, the gradually progressive symptoms of advancing incurable cancer. There is a small group of cases of cancer where treatment with radium has apparently, so far as our observations extend, been capable of eradicating the clinical manifestations of the disease. It would be premature to use the word "cured" in this connection, as the time elapsed is not sufficient to conform to the arbitrary three or five year limits commonly accepted in surgical literature, which are admittedly themselves time standards too brief to cover the infrequent but well-established cases of late recurrence. This group of cases includes the more superficial and less rapidly metastasizing forms of carcinoma, together with a few cases of the deeper and generally more serious types of disease which appear to be, for some unknown reason, individually more susceptible to radiation than the usual cases of the same character. In the large group of cases in which radium has marked beneficial effect as palliative treatment, and in the smaller group in which its effects are more permanent and complete in eradicating the clinical signs of the disease, radium has already justified the very considerable outlay necessary for its purchase, and the further difficulties and dangers of its effective administration.

The 1080 cases included in this report are those which entered the hospital in the 28 months from April, 1912, to January, 1916. Radium was not used for treatment here until September, 1913, but it was then applied to many of the cases which had entered the hospital before that time. 642 of the 1080 cases received radium treatment. The arbitrary date of January, 1916, was established in order that at least a year might have elapsed in every case reported before the results of treatment were assembled for study. The end results given, however, are carried up to date (January, 1917), and represent the results at periods from twelve to forty months after treatment was begun—an average of two years and two months.

During the period of time mentioned the Commission has been using only 235 milligrams of radium. This amount has since been greatly augmented through the kindness of friends of the University.

The tabular list of cases is as follows:

Carcinoma..... (A)		
Buccal Cavity.....(39A)		
Lip	39	
Palate	8	
Jaw (lower)	36	
Jaw (upper—antrum)	11	
Tongue and floor of mouth	33	
Tonsil	7	
Cheek (buccal surface)	5	
Total		139
Stomach, Liver, etc. (40A)		
Oesophagus	12	
Pharynx	9	
Gall-bladder and liver	2	
Pancreas	1	
Stomach	16	
Total		40
Peritoneum, etc. .....(41A)		
Peritoneum and omentum	2	
Intestine (colon)	5	
Rectum	9	
Total		16
Urinary Organs .....(45A)		
Bladder	3	
Total		3
G.-U., Male .....(45A)		
Prostate	5	
Penis	2	
Total		7
G.-U., Female .....(42A)		
Vagina	6	
Uterus	91	
Ovary	12	
Clitoris	1	

Vulva	2	
Total		112
Breast ..... (43A)		
Total		143
Skin, Face, etc. ..... (44A)		
Carcinoma	83	
Epidermoid carcinoma	58	
Rodent ulcer	34	
"Epithelioma"	21	
Total		196
Other Sites ..... (45A)		
Thyroid	7	
Neck glands	14	
Larynx	15	
Glands of groin, axilla, etc.	5	
Parotid	2	
Nasal mucosa	3	
Total		46
Sarcoma and Allied Tumors.. (F)		
Bone	16	
Soft parts	22	
Melanotic	8	
Endothelioma	2	
Brain tumor	9	
Myeloma	1	
Mixed tumors	4	
Hypernephroma	4	
Total		66
Benign Tumors		
Papilloma	31	
Miscellaneous	10	
Breast	5	
Keloid	9	
Naevus	15	
Total		70
Miscellaneous Conditions		
Keratosis senilis	33	
Tuberculosis	11	
Syphilis	11	
Lupus erythematosus	6	
Leukoplakia	8	
Leukaemia — Lymphatic .... 7; Myelogenous .. 22		29
Lymphoma	40	
Effects of radium	9	
Deafness	11	
Apprehension	14	
Fibrosis penis	3	
Miscellaneous diseases (not radium)	53	

Skin lesions—miscellaneous	6
Chronic inflammatory diseases	3
No diagnosis	5
Total	242
Grand Total	1080

Certain groups of cases of cancer of special organs or regions have been allotted to different members of the staff for analysis. These more detailed analyses will be published under separate titles. It will be sufficient in this introductory statement to formulate briefly the general estimate which has been formed of the value of radium treatment of cancer in its more common and important situations, and the evidence in support of these conclusions.

39A—CARCINOMA OF THE BUCCAL MUCOUS MEMBRANES—139 CASES.

(a) Cancer of the lip, 39 cases; 19 treated with radium; 4 with complete success; 4 with improvement, and 11 with no benefit. Squamous cell carcinoma in this situation is resistant to radium therapy. When the disease has metastasized to the regional lymph nodes no marked benefit from radium has been observed. Local recurrence, however, as in other superficial situations, can be affected favorably. It is our opinion that a grave responsibility rests on those who advocate radium treatment in preference to operation for cancer of the lip, in even its early stages.

Cancer of the palate, 8; tonsils, 7; buccal mucosa, 5; lower jaw, 36; upper jaw, 11; tongue and floor of mouth, 33—100 cases in all. Sixty-two of these received one or more treatments with radium; nine obtained some benefit from treatment. In the others the course of the disease was not materially affected. The best results were obtained in the cases of recurrent cancer of the jaw, where a neck dissection, performed at the time of the original radical operation, served to delay, if not to prevent, the glandular extension of the disease. In one such case local recurrence at the site of the original lesion on the jaw was destroyed with radium, and there has been no return of the disease in sixteen months. As a result of this experience we have recently treated a number of cases of otherwise inoperable mouth carcinoma by a primary neck dissection and subsequent radiation of the local tumor, and we are encouraged to hope that this method may prove effective in a certain number of cases not otherwise amenable to treatment.

40A—CARCINOMA OF STOMACH, LIVER ETC.—40 CASES.

(a) Carcinoma of the esophagus, 12 cases. Five received radium treatment, and of these one obtained some relief of symptoms, although no permanent good was accomplished.

(b) Carcinoma of the pharynx, 9 cases. All treated with radium, and with no material benefit with the exception of one case which showed temporary improvement under prolonged treatment.

(c) Carcinoma of the gall-bladder, 1; pancreas, 1; and liver, 1—3 cases. The gall-bladder case and the pancreas case both received radium treatment, without notable improvement.

(d) Carcinoma of the stomach, 16 cases. Only one received radium treatment, which was given three times, with psychic, but no obvious physical benefit to the patient.

41A—CARCINOMA OF THE PERITONEUM, ETC.—16 CASES.

(a) Carcinoma of the peritoneum and omentum, 2 cases. No benefit from radium.

(b) Carcinoma of the intestine, 5 cases. Two cases were given radium without benefit.

(c) Carcinoma of the rectum, 9 cases. In 5 radical operation was advised; 3 accepted this advice, and 2 of these are well four years and eight years* after operation; 3 received radium treatment, with but slight, if any, improvement in their condition.

45A—CARCINOMA OF THE URINARY ORGANS—3 CASES.

Carcinoma of the bladder, 3 cases. Two received radium treatment and 1 obtained some relief and is still under treatment.

45A—CARCINOMA OF THE MALE GENITO-URINARY ORGANS—7 CASES.

(a) Carcinoma of the prostate, 5 cases. Four received radium treatment. All are dead, but one of these obtained definite, but temporary, relief.

(b) Carcinoma of the penis, 2 cases, of which one was advised to undergo operation, and the other received radium treatment without benefit.

42A—CARCINOMA OF THE FEMALE GENITO-URINARY ORGANS—112 CASES.

(a) Carcinoma of the vagina, 6 cases. Four received radium treatment; all are dead, the average duration of life being six months from the time of beginning treatment.

(b) Carcinoma of the vulva, 2; clitoris, 1—3 cases. All received radium. In none has there been marked benefit from treatment.

(c) Carcinoma of the uterus, 91 cases. These cases form the basis of a special report by Drs. E. H. Risley and G. A. Leland, Jr., covering the period up to June, 1916, bringing the number of cases to 113. Ninety of these cases received radium treatment, as follows:

Group 1. Cases considered inoperable, and treated with radium, improved enough to justify radical operation: 5 cases; 3 living, 2 without recurrence at twelve and eighteen months after operation, and one case free from recurrence for two years after operation, then local recurrence, and now under treatment.

Group 2. Cases received for prophylactic treatment after radical hysterectomy: 5 cases; 2 free from recurrence twelve and fifteen months after operation; 2 recurrent cases, and 1 untraced, but free from recurrence eight months after operation.

Group 3. Recurrence after hysterectomy, 37 cases: 1 apparently free from disease; 2 doubtful, 5 living with recurrence, and 26 dead.

Group 4. Recurrence after curette and cautery: 21 cases; 4 living with recurrence and under treatment; 1 living and without evidence of disease nineteen months after beginning treatment, but since then untraced.

Group 5. Inoperable cases: 22; none free of disease. Average duration of life after beginning radium, twenty-two months.

Of the 91 cases, 5 living and apparently free of disease, six, twelve, twelve, fifteen and eighteen months after beginning treatment; 2 living and apparently free from disease eight and nineteen months after beginning treatment, but since then untraced. Of the 7, 2 were being treated

* Entered Collis P. Huntington Memorial Hospital for suspected recurrence, which did not exist. Original operation by Dr. C. A. Porter, 1909.

on a prophylactic basis, and showed, after operation, no evidence of recurrence. The other 5 were recurrent or inoperable cases.

(d) Carcinoma of the ovary, 12 cases; five received treatment with radium in varying amounts; 1 case showed temporary improvement, and died fifteen months after beginning treatment; the others showed no marked improvement under radium.

43A—CARCINOMA OF THE BREAST—143 CASES.

Radical operation was advised in 14 cases and accepted in 11 cases, 8 of which show no evidence of recurrence to date; 49 cases received radium, and 27 received x-ray treatment; 3 of the radium cases showed definite local improvement, but the internal progress of the disease was not affected. It is our opinion that x-ray treatment with massive doses offers more than radium in the palliative treatment of recurrent cancer of the breast.

45A—MISCELLANEOUS CARCINOMA—46 CASES.

(a) Carcinoma of the thyroid, 7; parotid, 2; axillary glands, 1; glands of groin, 2; cervical glands, 14; nasal mucosa, 3—29 cases. Nineteen received radium; only one of these cases, a carcinoma of the nasal mucosa, is apparently relieved of his disease. In all of the others the progress of the disease was not materially affected.

(b) Carcinoma of the larynx: 15 cases; 7 received radium treatment, and all are dead, although temporary improvement was observed in two cases.

44A—CARCINOMA OF THE SKIN, FACE, EARS, HANDS, ETC.—196 CASES.

Carcinoma, 83; epidermoid carcinoma, 58; rodent ulcer, 34; "epithelioma," 21. It is in cases of this superficial type that radium produces its most marked and beneficial therapeutic effects. Of the first group, carcinoma, 33, or 39%, show no evidence of return of the disease. Eight cases were operated upon without recurrence, and only 10 cases, or 12%, failed to obtain definite benefit from radium treatment. Of the 58 cases of epidermoid carcinoma, 15, or 25%, were relieved of all evidence of their disease, and only 9 cases, or 15%, failed to show definite benefit from radium treatment.

Of the 34 cases of the rodent ulcer (basal cell) type of carcinoma of the skin, 12, or 35%, were relieved of all symptoms, and 6 cases, or 17%, showed only temporary benefit, or none at all.

Of the 21 cases of "epithelioma," 9 were permanently relieved, 44%. Only one case obtained no benefit, and in one the benefit was only temporary.

To sum up these 196 cases of superficial carcinoma of the skin, in 69, or 35%, the disease was apparently destroyed, and in only 27, or 14%, did it appear to be so little affected by radium that the patient obtained no benefit. In all of the other cases improvement was manifest, although in a limited number of cases the disease recurred after apparent destruction by radium, and is again under treatment.

F—SARCOMA.

Bone, 16 cases; soft parts, 22; melanotic sarcoma, 8—46 cases.

Bone sarcoma, 16 cases; 3 treated with radium, of which 1 showed no improvement, 1 slight improvement, and 1 apparently relieved of all evidence of the disease.

Sarcoma of soft parts, 22 cases; 9 treated with radium—4 showed no improvement, and in 5 slight palliative benefit was obtained.

Melanotic sarcoma, 8 cases; three treated with radium with some benefit, but no permanent results.

MISCELLANEOUS TUMORS.

Endothelioma, 2; brain tumor, 9; myeloma, 1; mixed tumors, 4; hypernephroma, 4—total, 20.

In this miscellaneous group of tumors no material benefit from radium has been observed.

BENIGN TUMORS.

Papilloma, 31 cases. These occur in two groups: the papillomata of old persons, associated with keratoses, 25; and those of younger persons, 16. In old people papillomata are readily susceptible to radium treatment. Twelve of the 25, or 48%, were destroyed by radium, and 5 by caustics. Of the other group, only 2 were subjected to radium, and both of these successfully.

Keloid, 9 cases. Seven treated by radium, and all with benefit, although prolonged treatment may be necessary, and a strong application, made sufficient to cause a superficial burn, the fibrous tissue of keloid can be made to disappear with radium, leaving a flat and atrophic scar. The process is painful, but reasonably sure.

Naevus, 15 cases. Ten treated with radium, and all with benefit. Here long-continued mild treatments are required, but with perseverance the common port wine mark, as well as more prominent cavernous angiomata, can be made to diminish in color and size, and become less conspicuous.

MISCELLANEOUS CONDITIONS.

Leucoplakia Buccalis, 8 cases. Four treated with radium. The common superficial cases of leukoplakia can be made to disappear with radium. The process, however, is painful, as a superficial burn is required to eradicate the disease. It is to be advised only in the more productive cases, where the tissues are heaped up in papiliary masses, and for the simple milky glossitis type, fulguration, as carried out by Dr. C. G. Mixter, has, in our opinion, proved most effective.

Leukemia, 29 cases. Lymphatic, 7; myelogenous, 22. These cases form the basis of a special report by Dr. Francis Peabody. The lymphatic cases have shown themselves resistant to treatment with radium, while those of the myelogenous type almost invariably show beneficial effects from radiation of the spleen. The blood picture returns toward, if not to, normal, the spleen shrinks, the red blood cells increase, the patient's general health and strength improve, he gains weight, and he is often able to resume his regular occupation. It is rare, however, for the myelocytes entirely to disappear from the blood smear, and the disease is subject to remissions and recurrences. It would be premature to claim anything more permanent than a temporary remission of symptoms as a result of radium treatment, but this temporary remission appears to be more lasting and more certain than that obtained by other methods of treatment which have been advocated for this disease.

Lymphoma, 40 cases. These cases form the basis of a special report by Dr. C. C. Simmons and Dr. George Benet. Twenty-one of these cases received treatment with radium. Of this number, 18 were cases of typical Hodgkin's disease, 1 was lymphosarcoma, and 2 were malignant lymphoma in situations other than in the lymph nodes. In the 18 cases of the Hodgkin's type, radium treatment almost invariably produced marked regression of the lymphomatous glands, with shrinkage of the tumor masses, and improvement in the general condition. The regression was most marked in the more accessible glands (neck) and was not obtained in the deeper lesions (mediastinum). Furthermore,

the regression was almost invariably temporary, and sooner or later recurrence of the disease took place. It is our belief that more persistent and heavier treatment, especially of the mediastinal glands, may yield more satisfactory results. Of the lymphosarcoma group, one case, although glands are still present, has received marked benefit from radium treatment, and is now in good condition eighteen months after beginning treatment. Of the 2 malignant lymphoma cases, both have apparently obtained a disappearance of their disease,—one of the palate and one of the rectum. The palate case recurred, but the recurrence also disappeared, and the case is now thirty-three months without recurrence. The rectal case has been free of disease for twenty-four months.

It would appear that tissue of the lymphoma type was especially susceptible to the action of radiation, and the use of radium in such cases is to be advised.

Keratosis Senilis, 33 cases. One of the lesions most amenable to radium treatment. Twenty cases, or 60%, were relieved of the disease, one case recurred and received further treatment, and only two proved entirely resistant to radiation. One or two mild applications are usually sufficient to eradicate the lesions, without the production of a burn, or, indeed, any material discomfort to the patient.

SUMMARY.

As a result of the use of about 235 milligrams radium in the treatment of 642 cases of cancer and allied conditions at the Collis P. Huntington Memorial Hospital, from September, 1913, to January, 1916, the following conclusions are justified.

1. Many cases of advanced, inoperable or recurrent cancer may be given benefit by treatment with radium.

2. In such cases the relief may include one or more of the following advantages: Relief of pain, diminution of discharge in the size discharges less offensive, relief of hemorrhage, diminution in the size of tumor masses, even to their total disappearance; and the improvement in the general condition of the patient. To these must be added the undoubtedly beneficial psychic effect upon the patient.

3. In a very small number of advanced and apparently inoperable cases, improvement may occur such as to permit a radical operation to be performed.

4. In a certain proportion of cases of superficial non-metastasizing types of cancer (about 35%) and in a much smaller number of cases of metastasizing cancer, radium is capable of destroying the clinical manifestations of the disease. Time has not elapsed sufficient to report these cases as "cured," and they are being kept under observation. In a limited number of cases, recurrence, after apparent destruction of the lesion, has taken place. In certain situations, as on the eye-lids, radium treatment of these lesions is to be preferred to operation.

5. In keratoses, papilloma and other benign skin diseases regarded as "precancerous," radium is effective in destroying the clinical manifestations of the disease in from 48 to 60% of cases.

6. In myelogenous leukemia, the beneficial effects of radium are pronounced, and although recurrence of symptoms may take place, the clinical advantages of radium therapy are very marked.

7. In malignant lymphoma, lymphosarcoma, and Hodgkin's disease, the lesions appear to be especially sensitive to radiation, and definite, though temporary, benefit is obtained. When in accessible situations, it

would appear that the disease could be controlled by radiation for a considerable period of time.

8. In the treatment of many other tumors and diseases radium has been used with benefit depending largely upon the extent of the disease, its depth in the tissues, and the practical ability to apply sufficient radiation to modify or destroy tissue or tumor growth. Among the conditions in which radium treatment has proved of special value may be mentioned: recurrent or inoperable carcinoma of the cervix, or of the body of the uterus, Hodgkin's disease and malignant lymphoma, myelogenous leukemia, inoperable squamous cell carcinoma of the tongue, jaw and buccal mucous membranes, in non-metastasizing epidermoid cancer and in the more benign lesions of keratoses, papilloma, and other so-called precancerous conditions.

9. Radium therapy has proved, so far, to be of little benefit in recurrent carcinoma of the breast, carcinoma of the stomach and intestine, carcinoma of the glands of the neck, by extension from cancer of the tongue, mouth and lip, and in general in deeply seated metastatic extension of cancer from any region.

10. The use of radium in prophylaxis of recurrence after radical operation, for the cure of cancer, is not advised. Where serious doubt exists as to the complete removal of the primary tumor, and where the location of the suspicious area is superficial and accessible, and of small extent, radium may be used with benefit, but where a large area is to be considered, as after operation for breast cancer, the difficulties of covering the whole area with sufficient radiation are such that the treatment is not to be recommended.

11. The combination of radium therapy and operation, by which a tumor, otherwise inoperable, is excised as thoroughly as possible, the remaining tissues cauterized, and subsequently subjected to radiation, has yielded satisfactory results in several cases. This method of procedure is especially adapted to the more advanced cases of rodent ulcer, involving the face. After a period of radiation and observation of the open, granulating wound, extending over several months, secondary plastic operations have been performed to close the defects, and the results, up to the present time, in a very small number of cases, have shown no return of the disease.

12. Of 642 cases treated with radium in this series, 354, or 55%, received definite benefit.

13. Although many cases of advanced carcinoma show no appreciable benefit from radium treatment, it is also true that in no case yet observed has radium appeared actually to accelerate the growth of tumor tissue. Patients have suffered pain and inconvenience from the effects of radium burns in certain instances, but these have been of a temporary character. The constitutional effects of heavy doses of radium are unpleasant, and severe nausea and depression may occur; but these, also, are chiefly temporary in character. With continued and excessive dosage, very profound constitutional effects may be obtained. A serious diminution in the number of white cells in the blood is observed after continued heavy dosage. This is a more lasting phenomenon, and may be of serious importance in relation to the patient's resistance to infection. On this subject we are not, as yet, ready to report. In no other respect have we found radium to exert an unfavorable action upon the patient.

14. The considerable expense of purchase and the difficulties and dangers of administration of radium therapy are more than justified by the results obtained.

REVIEWS AND ABSTRACTS

Edward H. Risley, M. D., (Boston), and George A. Leland, Jr., M. D., (Boston). Report of Treatment of Carcinoma of Cervix at the Huntington Hospital for Period of Four Years. The Boston Medical and Surgical Journal, CLXXVII, pp. 891-894, Dec. 27, 1917.

"This paper is a report of the results obtained in the treatment by radium of a series of 113 cases of carcinoma of the uterus at the Huntington Hospital from January, 1912, to June, 1916, inclusive."

"In order to form a proper estimate of the value of treatment it is necessary to divide the cases into several definite groups; otherwise, statements in regard to results in cancer of the uterus are of little value unless we consider the groups separately."

GROUP I. "Cases of border-line operability in which pre-operative radium treatment aims at a reduction in the size and fixation of the mass, rendering the chance of total extirpation more promising."

GROUP II. "Cases accepted for prophylactic radiation following radical hysterectomy."

GROUP III. "Those of recurrence following hysterectomy."

GROUP IV. "Those of recurrence or continuation following curettage or cauterization."

GROUP V. "Those which were primarily and unquestionably inoperable. There have been no cases accepted for radium treatment alone where radical hysterectomy seemed possible."

"Case histories have been examined especially with the idea of forming some estimate of what the first symptoms were that brought the patient to her physician, of what type the local physical signs and findings were, of forming as nearly as possible a probable prognosis, of getting an idea as to what the general effects of radium treatment were, and of determining in what percentage of cases a positive pathological report was made."

"In the early months of the hospital five cases were treated by injections of ascitic fluid. Twenty-three cases were examined, but for some good reason were not treated and are not included in the study of this series. Ninety cases were taken as a basis of study. All of these received radium treatment."

"It has been very gratifying to find that a large number of our cases are referred from other hospitals, both for consultation and for treatment. It was found that fifty-six cases were referred from other institutions, and thirty-four from physicians elsewhere. The oldest case treated was 68, the youngest 30, and the average about 50 years."

"First symptoms were reported as flowing in 84 cases, pain in 5, and amenorrhea in 1. Local physical signs were recorded as follows: ulceration only, 3 cases; sinus, 5 cases; implantation on vaginal wall, 21 cases; implantation on abdominal wall or in abdomen, 3 cases; glandular metastases (at time of admission), 5 cases; cervix nodular (plus other signs), 19 cases; mass in vault, 24 cases; ulcerated or necrotic mass, 35 cases; crater, 25 cases; extension to vaginal walls, 28 cases; bleeding of

greater or less degree, 42 cases; extension to broad ligaments, 33 cases; pelvic masses, 7 cases; involvement of bladder, 6 cases; involvement of rectum, 4 cases; fixation of uterus or broad ligaments, 13 cases. Thus it is evident, therefore, that cases of all grades of severity were accepted for treatment, and no effort was made to pick out only the probably favorable ones."

"The prognosis was stated as favorable, probably favorable, or border-line in 16 cases; unfavorable in 39 cases; very unfavorable or hopeless in 22 cases; and not stated in 13. Of these reported as favorable, there are today 3 alive without recurrence, 2 with a question of recurrence, 4 not doing well (disease progressing), 6 dead, and 1 lost track of. All of the cases reported as unfavorable are dead except one, as are all of the hopeless cases."

"Pathological reports made, either at the Huntington Hospital, or before entrance, were recorded in 38 cases. No pathological report was made, or at least was not recorded, in 52 cases. This small number of pathological reports is accounted for partly from lack of accurate data obtainable from patients coming to us from remote regions and partly because of the policy of the hospital not to cut into suspicious tissues because of the very real danger of dissemination of the disease. Practically all of the cases, however, have been unmistakably carcinoma as far as clinical signs go. The disease was reported as carcinoma in 12 cases, adeno-carcinoma in 7 cases, squamous cell in 9 cases, epithelial in 3 cases. Specimen taken but no pathological report in 7 cases."

"In general the effects of the radium treatment are recorded as follows: temporary local benefit, 44 cases; much improved, 5 cases; entire relief from pain, 5 cases; some relief of pain in all but a few complaining of this symptom; complete relief from bleeding, 14 cases; healing of ulceration, 11 cases; decrease in the size of the growth, 8 cases; no improvement at all in 13 cases; increase in the growth (some rapid) in 30 cases; fistula (vesico-vaginal) developed in 2 cases; mass made more movable in 8 cases.

Mortality. There were 2 deaths from disease other than carcinoma, —1 from pneumonia and 1 from pelvic abscess. The results remain unknown in spite of a very efficient follow-up system in 7 cases. The total mortality dated Feb. 1, 1917, is 62 cases. There are 21 cases in this series still under treatment for observation."

"The radium has been applied:

'Per vaginam in 89 cases.

"Per rectum in 1 case.

"Over abdominal scar in 1 case.

"Over inguinal glands in 2 cases.

"The dose in this series has averaged less than 1000 millicurie hours."

"Hemorrhage has been easier to control than pain because the superficial ulcerations are more readily affected than the deep extensions. The latter have been rarely improved and if so only temporarily. The healing of the vaginal disease is often accompanied by contraction of the vagina, which renders difficult satisfactory apposition of radium to the persisting deeper extensions. Long exposure with screening of the superficial radium rays has been preferable to short exposures without screening, except in rare instances of very superficial vaginal recurrent lesions."

GROUP I. "The number of cases treated as a preliminary to operation is very small—only 5. It is probable that pre-operative radium to

the cervix and vault and over the abdomen acts in some measure like the Percy cautery in that it kills some cancer cells, and allows some softening of the mass without scattering cancer cells, checks foul discharge, and leaves a somewhat cleaner mass to be removed."

"Many operators affirm that operation soon after radiation is much more difficult because of greatly increased venous bleeding, and that the operative difficulties are increased, also because of the foundation of adhesions and fibrous tissue. We believe, however, that pre-operative treatment is a line that should have the benefit of much further trial. We are also positive in our belief that none of these cases should be allowed to go without thorough post-operative radiation as well. It is never possible to tell, even in the widest surgical direction, when all cancerous cells have been removed, therefore, these cases which were of the border-line type would seem to be the type in which post-operative prophylactic radiation was the logical procedure."

"There were five cases of border-line operability (as determined by more or less fixation of the broad ligaments or uterus), in which, after a certain amount of the radium treatment, the mass became more movable and which were then considered operable. Of these, three are alive today, one eighteen months after operation and without symptoms, one twelve months after operation and without recurrence, one twenty months after operation but with local recurrence. Two are dead,—one died three weeks after operation (cause not stated), and one free from disease for two years after operation, then recurrence and death after four months of radium treatment. If this method is given extensive trial there may result numbers of seemingly inoperable cases which will be given a chance at operation and a possible further escape from extension of the disease."

Group II. "The policy of the hospital in the early days of treatment was to wait for definite signs of recurrence before attempting anything in the way of prophylactic radiation. With the advent of greater familiarity with the conditions under which recurrence takes place and the examination of the great number of suspicious cases, and also with the increasing realization that it is within no man's power to determine, even in the most extensive and radical removal of glandular areas, when all cancerous cells have been removed, it has gradually become our policy to accept for prophylactic radiation after hysterectomy these cases in which, in the surgeon's opinion, the disease probably was not entirely eradicated."

"In view of the reports from other workers with radium and our increasing efforts to deal with precancerous conditions, it seems rational that we should more and more frequently treat all our malignant disease post-operatively by prophylactic radiation, either with radium or x-ray. This is certainly a logical procedure, and it is our hope that the profession in general will recognize this and send cases directly after operation for a course of prophylactic radiation."

"Our series shows an altogether too small number of this type of cases—five in all; of these, three are now alive and without disease fifteen months after operation and one with disease twelve months after operaton. One case is not traced to date, but was free from disease for eight months after operation. One case died of recurrence fourteen months after operation."

Group III. *Post-operative or Recurrent Cases.*—"The follow-up system in all cases, now becoming more and more effective in our hos-

pitals, is already producing results in that we are beginning to get post-operative cases back for observation regularly and are able to treat them vigorously at the very first suspicion of any recurrence if for any reason we do not see fit to institute prophylactic treatment. The future outlook for such cases seems good. Early radical operation with early radiation of recurrence ought to produce greatly better results."

"It can be pretty definitely stated that very superficial or small recurrence in the vault of the vagina, especially those which manifest themselves as superficial ulcerations, are practically always favorably affected by the radium. Dense nodular recurrences are more difficult to penetrate and more often accompanied by lymphatic involvement and hence less favorable. Recurrences after hysterectomy generally occur in the vagina, either along its walls or in the vault in the scar of operation. If taken early these cases generally respond quickly to radium."

"This group comprises 37 cases recurrent after hysterectomy—16 after the Wertheim operation and 21 after hysterectomy of type not stated. Three of these have not been traced. Eight are alive today and without disease, 2 with a question of recurrence and five with definite recurrence. Twenty are dead, and the average duration of life after operation and the beginning of radium treatment was eight months.

GROUP IV. "This comprises recurrent cases of all stages of recurrence; a great many of them being advanced and with large masses of malignant tissue to deal with,—a class carrying a prognosis almost equally as bad as the originally inoperable cases. These cases which return for radiation early after first suspicion of disease can definitely be given a hopeful prognosis of a considerable prolongation of life, with much relief from pain and delay in the progress of the disease. The least favorable group of cases is that in which there is recurrence or continuation of the disease following curettage or cauterization."

"Practically all of these cases were received anywhere from two weeks to eight months after the palliative operation, and in almost every case there had been steady progress of the disease since the operative procedure. These cases have not done particularly well. It is believed that, on the other hand, if cases can be thoroughly cauterized, getting rid of practically all of the diseased area, a real crater formed of the cervix and radium immediately placed in the cavity, better results can be obtained. There were 21 cases. Two are not traced. One is alive and without recurrence nineteen months after beginning radium, and three were lost sight of. Four others are alive, but all with disease with an average of ten months after beginning radium treatment. Fifteen are dead, with an average duration of eight months after institution of treatment."

GROUP V. "As would be expected, every clinic shows a larger number of inoperable cases sent for radiation than any other type of case. A general statement only in regard to this type of case can be made, as follows. Probably only palliation can be hoped for. A cure is rarely to be expected in the light of our present knowledge of radium technic. There are enthusiasts who offer more hopeful opinions, but the mass of cases treated is not yet large enough to be at all convincing. However, much relief from distressing symptoms can be brought about in this unfavorable type of cases, even if extension into the broad ligaments and lymphatics destroys all chance of cure."

"There are three things that radium can do in practically every case.

It can check hemorrhage, stop to a large extent foul discharge (of course depending on the size of the growth), and in many cases it does control pain. We never predict to patients that we surely can do any of these things, but we can give them a reasonable assurance that such will be the case. Certainly energetic radium treatment in the inoperable case offers more in the way of relief from symptoms than the use of the red hot cautery and curettage as formerly employed, and numerous writers believe the prolongation of life is greater."

"In this connection, it would seem wise in making any statement in regard to radium, as well as any other non-operative form of treatment, to be conservative and consider well all the factors entering into the improvement of the patient. The temporary improvement seen in many cases is undoubtedly due, in some instances, to the recuperation of the system dependent on checked bleeding. The temperature arising from the absorption of toxic products is lowered and a general improvement is felt by the patient, who thereby gains new courage from the psychic as well as the physical factors involved."

"This group includes 22 cases comprised entirely of definitely inoperable cases; only 1 has not been traced. There are 3 alive, all with disease with an average duration since starting radium treatment of 22 months. These are interesting figures, showing the apparent retardation of growth and bettering of general conditions following radium in this type of case. Apparently the original growth is of a more slowly progressing nature under radium in these cases than recurrent growths after hysterectomy. There are 18 cases dead, all with disease with an average duration of life after the beginning of radium treatment of nine and a half months."

"A summary of these grouped cases shows:

"Five without disease—one, 18 months; one, 15 months; two, 12 months; one less than 6 months."

"Twenty-one alive (two with question of disease less than 6 months)—seven not traced but two free from disease eight or nine months after it started; fourteen with disease."

"Sixty-two are dead."

"The points of interest and value brought out in this analysis are as follows: Much symptomatic relief can be expected from radium treatment, especially in the checking of hemorrhage and alleviation of pain. Prophylactic radiation immediately following hysterectomy is a logical, safe and advisable procedure and should reduce the number of recurrences. The treatment of early recurrences offers a fair prognosis. Late treatment offers little but alleviation of symptoms and but little retardation of growth. Inoperable cases are benefited by radium and the period of life is somewhat prolonged. Radium should be given more extended and earlier trial in these cases. It is believed that every case operated on should be required to report for observation once a month for the first year and once in three months for the second year and at frequent intervals for each succeeding year. Only in this way can early recurrences be detected and early institution of radium treatment be started."

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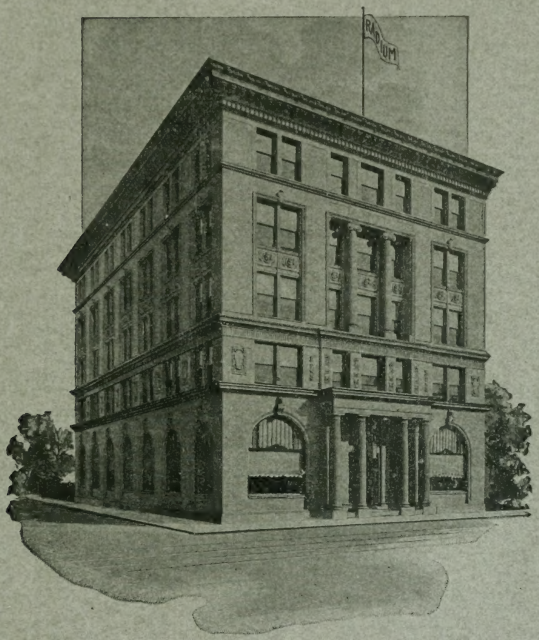

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